# PROTOCOL SYNOPSIS – BMT CTN PROTOCOL 0101

## A Randomized Double-blind Trial of Fluconazole versus Voriconazole for the Prevention of Invasive Fungal Infections in Allogeneic Blood and Marrow Transplant Recipients

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**Accrual Objective:** Allogeneic blood or marrow transplant recipients and cord blood recipients in children under the age of 12 will be targeted for accrual. Per study arm, approximately 300 recipients (a total of 600 recipients) will be accrued.

**Accrual Period:** The estimated accrual period is three years.

**Study Design:** The study is designed as a Phase III, randomized, double-blind, multicenter, prospective, comparative study of fluconazole versus voriconazole in the prevention of fungal infections in allogeneic transplant recipients. Recipients will be stratified by center and donor type (sibling vs. unrelated) and will be randomized to either the fluconazole or voriconazole arm in a 1:1 ratio.

**Primary Objective:** The primary objective is to compare the fungal-free survival rates between the two study arms through Day 180.

**Secondary Objectives:** The secondary objectives will be to compare the frequency of invasive fungal infection, time to invasive fungal infection, survival rate, duration of amphotericin B or caspofungin therapy for possible invasive fungal infection, time to neutrophil and platelet engraftment, time to and severity of acute and chronic GVHD, and to perform exploratory analyses of quantitative aspects of the galactomannan assay. The relative safety of the two antifungals will also be assessed through the collection of adverse events and routine laboratory monitoring.

**Eligibility Criteria:** Recipients must be diagnosed with leukemia or myelodysplastic syndrome (MDS). Lymphoma patients with chemosensitive disease and a related donor are eligible. Recipients must receive a myeloablative, 5/6 or 6/6 HLA-matched allogeneic blood or marrow transplant, be two years of age or older, have adequate physical function and give signed informed consent prior to enrollment.

**Treatment Description:** Recipients will begin the study drug on Day 0 (day infusion of stem cell product is initiated). The development of any fungal infection during prophylaxis will be classified according to revised EORTC/MSG definitions (see Tables 3.1.1a and 3.1.1b). Study drug will be continued until Day 100 post-transplant or until invasive infection occurs, or the recipient develops a Grade III or IV toxicity attributable to the study drug. For recipients of any type of graft receiving at least 1.0 mg/kg/day of prednisone (or equivalent steroid dose) on Day 90-100 or for recipients of T cell depleted grafts, receiving immunoprophylaxis post-transplant or having CD4+ counts < 200/μL on Day 90-100, study drug will be continued until Day 180.

**Study Duration:** Recipients will be followed for a minimum of one year post-transplant. Fluconazole or voriconazole will be taken (depending on randomization arm) beginning at Day 0 of transplant for at least 100 days (or longer as specified above).